* Paul Schulwitz please. Please review attachments with search request marks.

108239

Access DB#

SEARCH REQUEST FORM

Scientific and Technical Information Center

(STIC)

Requester's Full Name: Molly Ceperley Examiner #: 59757 Date: 11/13/03

Art Unit: 1641 Phone Number 30 8-4239 Serial Number: 10/035,594

Mail Box and Bldg/Room Location: 8D15 Results Format Preferred (circle): PAPER DISK E-MAIL

→ 7E12

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____ See bibliographic data sheet attached.

Earliest Priority Filing Date: 12/29/00

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search for the diketopiperazine compounds of claim 1. From what I've seen of the prior art, I think you can search the basic structure including the R^4 group (maybe also the R^1 group) and not get too many hits. Please let n be 1-6.

****

STAFF USE ONLY

Searcher: Kurt Luckenbach

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: 11/18

Date Completed: 11/19

Searcher Prep & Review Time: 30

Clerical Prep Time: _____

Online Time: 41

Type of Search

NA Sequence (#) _____

AA Sequence (#) _____

Structure (#) 1

Bibliographic _____

Litigation _____

Fulltext _____

Patent Family _____

Other _____

Vendors and cost where applicable

STN 249

Dialog _____

Questel/Orbit _____

Dr.Link _____

Lexis/Nexis _____

Sequence Systems _____

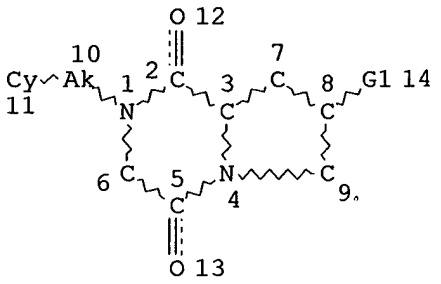
WWW/Internet _____

Other (specify) _____

PTO-1590 (8-01)

Considered 11/20/03 MTE

d que l6
L1 STR



VAR G1=O/15
NODE ATTRIBUTES:
NSPEC IS RC AT 15
CONNECT IS E2 RC AT 10
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC SAT AT 10
GGCAT IS UNS AT 11
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L2 68 SEA FILE=REGISTRY SSS FUL L1
L6 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L2

=> d ibib abs hitstr 16 1-5

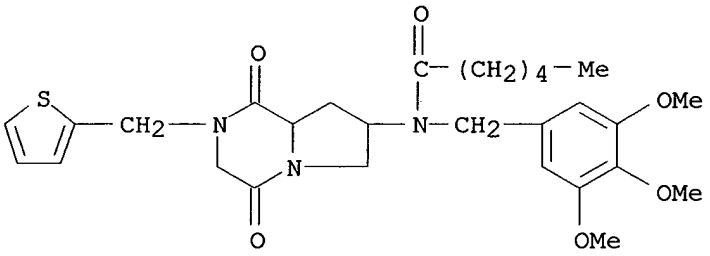
L6 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:418214 HCAPLUS
DOCUMENT NUMBER: 139:159195
TITLE: Quality Control in Combinatorial Chemistry: Determination of the Quantity, Purity, and Quantitative Purity of Compounds in Combinatorial Libraries
AUTHOR(S): Yan, Bing; Fang, Liling; Irving, Mark; Zhang, Sue; Boldi, Armen M.; Woolard, Frank; Johnson, Charles R.; Kshirsagar, Tushar; Figliozzi, Gianine M.; Krueger, Clinton A.; Collins, Nathan
CORPORATE SOURCE: ChemRx Division, ChemRx Division Discovery Partners International Inc., South San Francisco, CA, 94080, USA
SOURCE: Journal of Combinatorial Chemistry (2003), 5(5), 547-559
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The quality of combinatorial libraries dets. the success of biol. screening in drug discovery programs. The authors evaluate and compare various methods for measuring identity, purity, and quantity (yield) of

combinatorial libraries. Determination of quant. purity reveals the true library
quality and often indicates potential quality problems before full-scale library production The relative purity can be determined for every member in a large library in a high-throughput mode, but must be cautiously interpreted. In particular, many impurities are not observable by relative purity measurements using detectors such as UV214, UV254, and evaporative light-scattering detection. These invisible impurities may constitute a significant portion of the sample weight TFA, plastic exts., inorg. compds., and resin washout are among these impurities. With compelling evidence, the authors reach a conclusion that purification is the only way to remove invisible impurities and improve the quant. purity of any compound even though some compds. may have a high relative purity before purification

IT **564486-14-2P**
RL: ANT (Analyte); CPN (Combinatorial preparation); ANST (Analytical study); CMBI (Combinatorial study); PREP (Preparation)
(quality control compound; determination of quantity, purity, and quant. purity
of compds. in combinatorial libraries)

RN 564486-14-2 HCAPLUS

CN Hexanamide, N-[octahydro-1,4-dioxo-2-(2-thienylmethyl)pyrrolo[1,2-a]pyrazin-7-yl]-N-[(3,4,5-trimethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

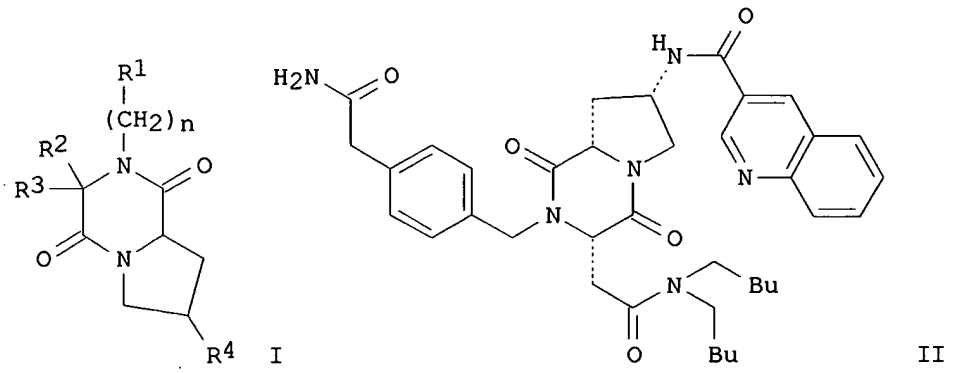
L6 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:615615 HCAPLUS
DOCUMENT NUMBER: 137:169547
TITLE: Preparation of 1,4-dioxooctahydropyrrolo[1,2-a]pyrazines as TNF-α inhibitors for treatment of inflammation
INVENTOR(S): Boyce, Jim P.; Howbert, Jeffry J.; Tabone, John C.
PATENT ASSIGNEE(S): Celltech R & D, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062797	A2	20020815	WO 2001-US49576	20011228

this applicn

Searched by P. Ruppel

WO 2002062797 A3 20021219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002187984 A1 20021212 US 2001-35594 20011228
PRIORITY APPLN. INFO.: US 2000-259359P P 20001229
OTHER SOURCE(S): MARPAT 137:169547
GI



I II

AB The title diketopiperazines I [wherein R1 = (hetero)aryl ring; R2, R3, R5, R6, and R7 = independently H, (hetero)aryl, (hetero)alkyl, carbocycle aliphatic ring, or heterocycle aliphatic ring; n = 1-3; R4 = OR5 or NR6R7; or NR6R7 = heterocycle aliphatic ring; or optical isomers, diastereomers, enantiomers, pharmaceutically acceptable salts thereof in isolation or mixture] were prepared For example, 1,4-dioxooctahydropyrrolo[1,2-a]pyrazine amide II was prepared in a 10-step synthesis in 5.6% overall yield involving condensation and cyclization reactions. II functioned as inhibitors of TNF-α-induced apoptosis with IC50 = 8 μM, TNF-α-induced expression of BFK-B with IC50 = 30 μM, and binding of IL-8 or GRO-α to CXCR1 or CXCR2 with 10-30% inhibition at 20 μM. The synthesis of I, their use in inhibiting cellular events such as those involving NFK-α, NFK-β and in the treatment of inflammation events, a combinatorial library of diverse 1,4-dioxooctahydropyrrolo[1,2-a]pyrazines, and process for their synthesis as a library and as individual compds were reported. In particular, I are disclosed including their synthesis and use in cellular events such as activation of the transcription factor, nuclear factor, TNF-α, TNF-β, and also apoptosis.

IT **447405-84-7P 447405-89-2P 447405-90-5P 447405-91-6P 447405-92-7P 447405-93-8P 447405-94-9P 447405-95-0P 447405-96-1P**

447405-97-2P 447405-98-3P 447405-99-4P
447406-00-0P 447406-01-1P 447406-02-2P
447406-03-3P 447406-04-4P 447406-05-5P
447406-06-6P 447406-07-7P 447406-08-8P
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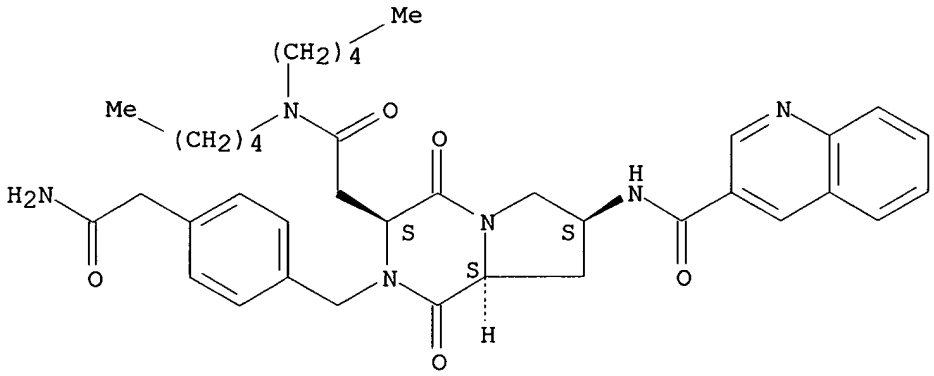
447406-12-4P 447406-13-5P 447406-14-6P
447406-15-7P 447406-16-8P 447406-17-9P
447406-18-0P 447406-19-1P 447406-20-4P
447406-21-5P 447406-22-6P 447406-23-7P
447406-24-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TNF-α inhibitor; preparation of pyrrolo[1,2-a]pyrazines as TNF-α inhibitors for treatment of inflammation)

RN 447405-84-7 HCAPLUS
CN 3-Quinolinecarboxamide, N-[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-3-[2-(dipentylamino)-2-oxoethyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]- (9CI) (CA INDEX NAME)

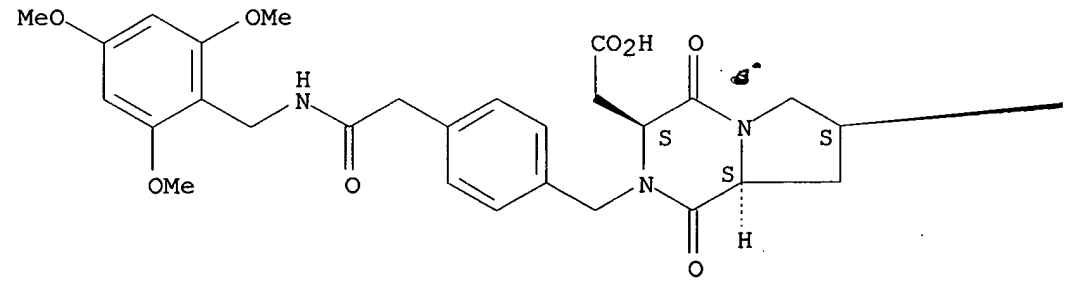
Absolute stereochemistry.



RN 447405-89-2 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 7-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

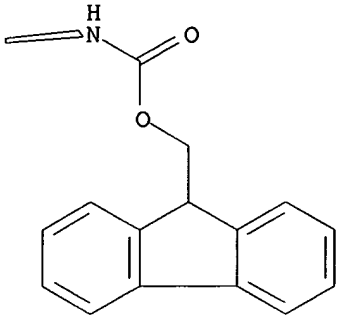
Absolute stereochemistry.

PAGE 1-A



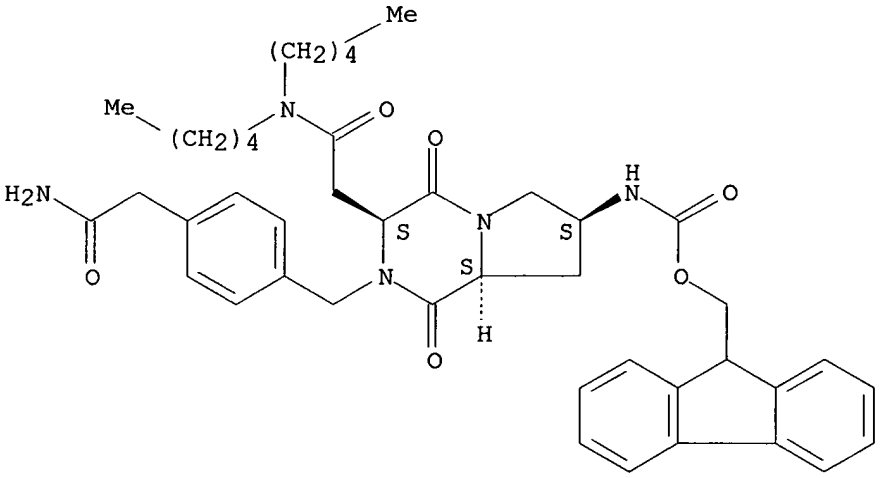
Searched by P. Ruppel

PAGE 1-B



RN 447405-90-5 HCAPLUS
CN Carbamic acid, [(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-3-[2-(dipentylamino)-2-oxoethyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

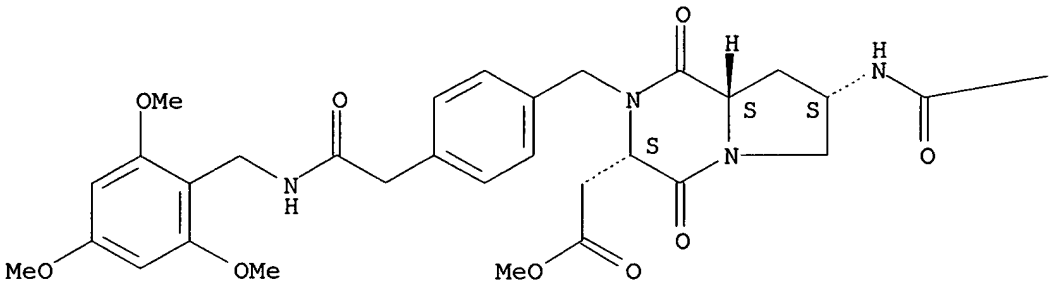
Absolute stereochemistry.



RN 447405-91-6 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, octahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]-7-[(3-quinolinylcarbonyl)amino]-, methyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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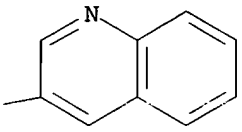
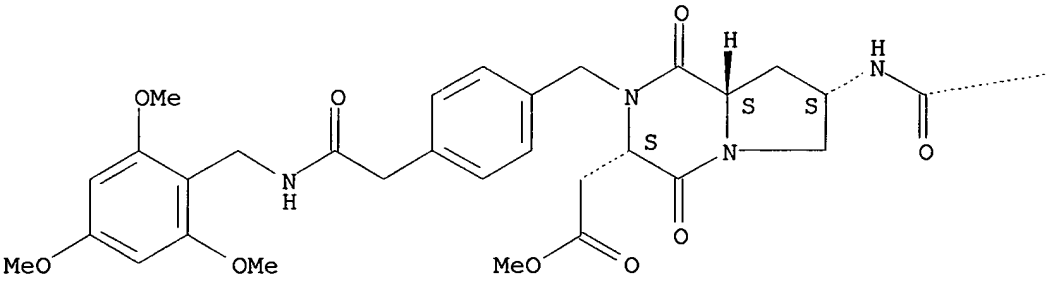


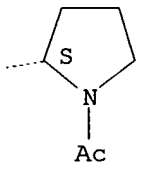
RN 447405-92-7 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 7-[[[(2S)-1-acetyl-2-pyrrolidinyl]carbonyl]amino]octahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]-, methyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



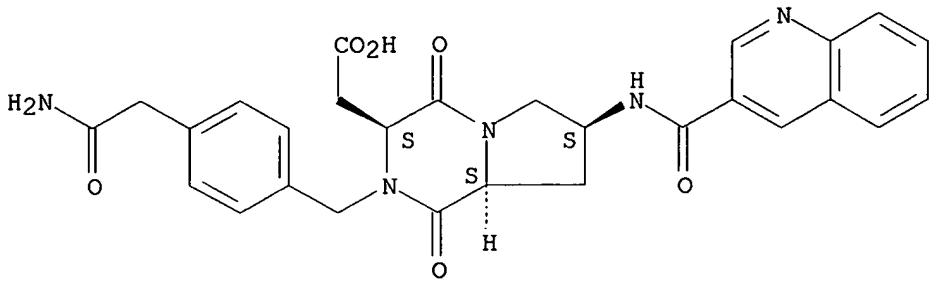
PAGE 1-B



RN 447405-93-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 2-[[4-(2-amino-2-

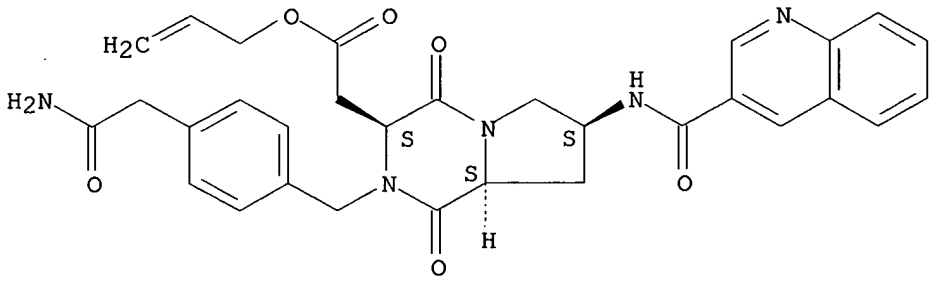
oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[(3-quinolinylcarbonyl)amino]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



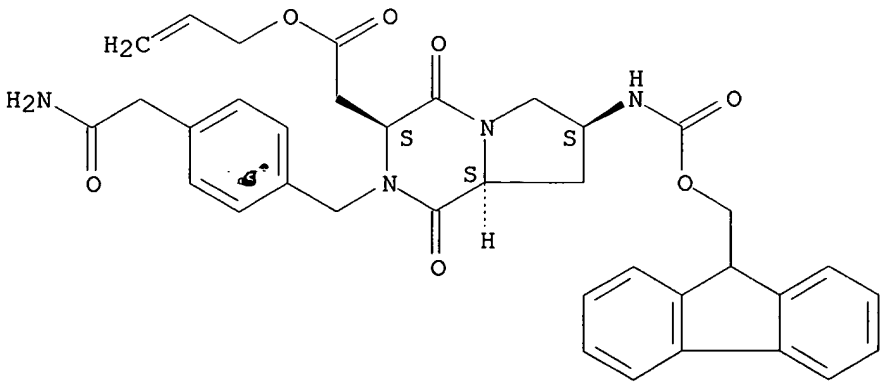
RN 447405-94-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[(3-quinolinylcarbonyl)amino]-, 2-propenyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 447405-95-0 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-7-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-1,4-dioxo-, 2-propenyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

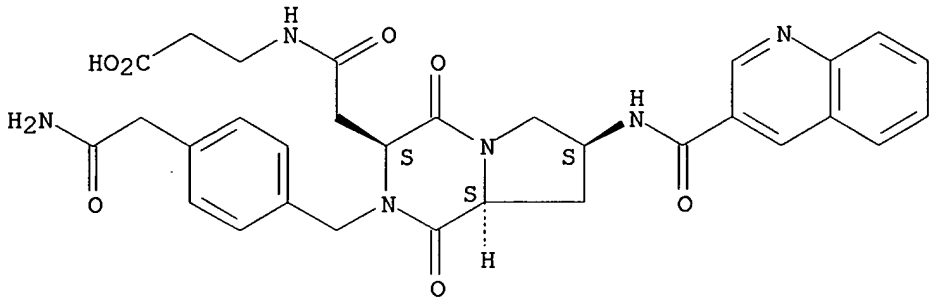
Absolute stereochemistry.



Searched by P. Ruppel

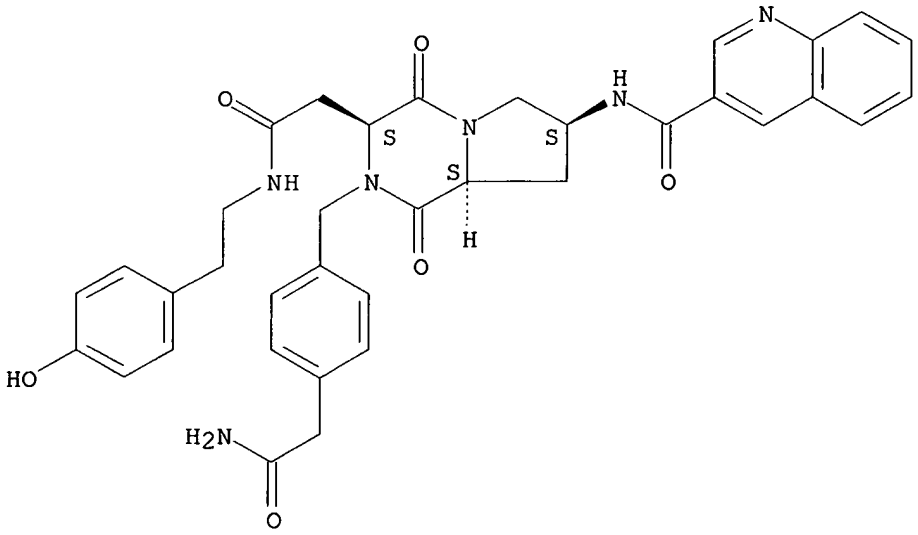
RN 447405-96-1 HCAPLUS
CN β-Alanine, N-[[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[(3-quinolinylcarbonyl)amino]pyrrolo[1,2-a]pyrazin-3-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



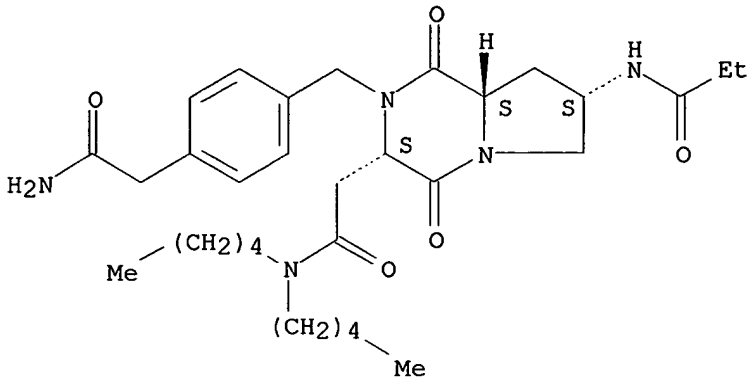
RN 447405-97-2 HCAPLUS
CN 3-Quinolinecarboxamide, N-[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-3-[2-[[2-(4-hydroxyphenyl)ethyl]amino]-2-oxoethyl]-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



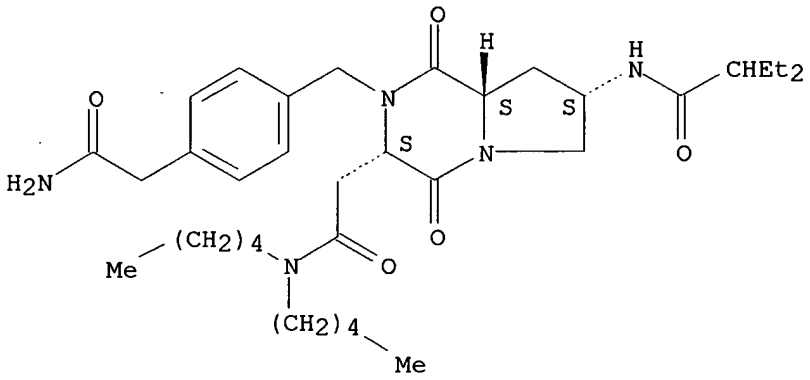
RN 447405-98-3 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[(1-oxopropyl)amino]-N,N-dipentyl-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



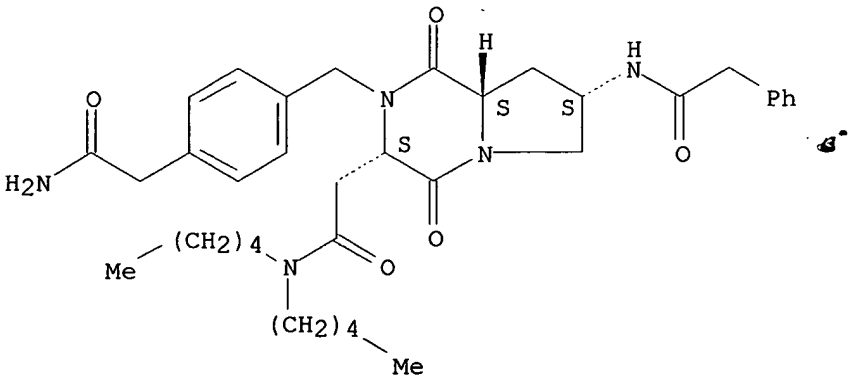
RN 447405-99-4 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-7-[(2-ethyl-1-oxobutyl)amino]octahydro-1,4-dioxo-N,N-dipentyl-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 447406-00-0 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-N,N-dipentyl-7-[(phenylacetyl)amino]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

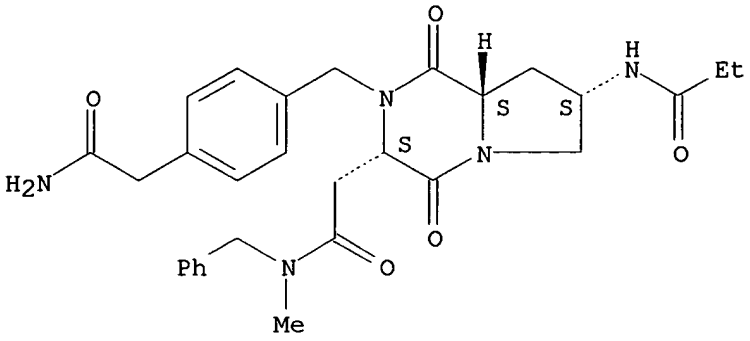
Absolute stereochemistry.



Searched by P. Ruppel

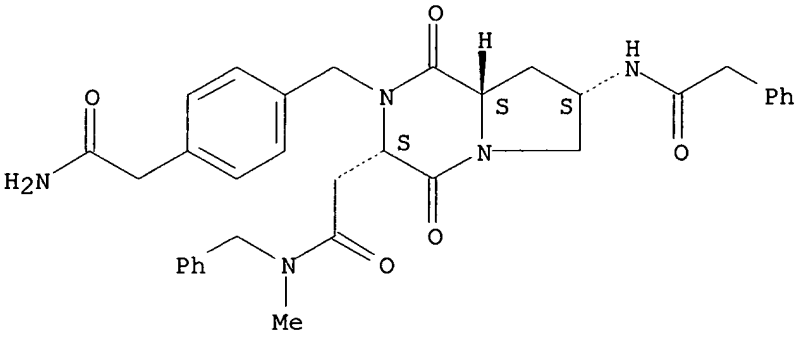
RN 447406-01-1 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-N-methyl-1,4-dioxo-7-[(1-oxopropyl)amino]-N-(phenylmethyl)-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



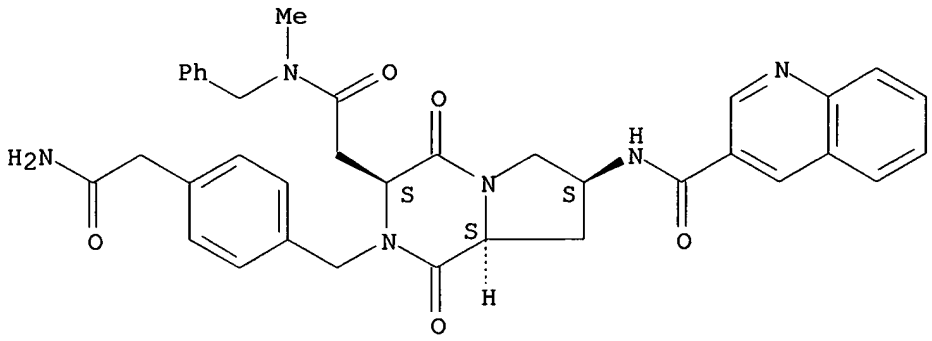
RN 447406-02-2 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-N-methyl-1,4-dioxo-7-[(phenylacetyl)amino]-N-(phenylmethyl)-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



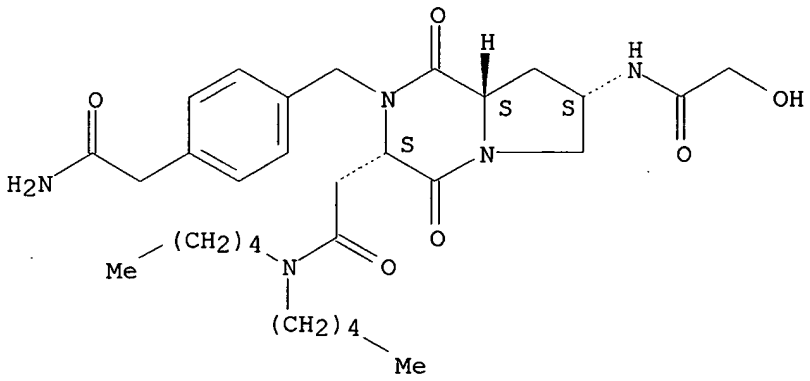
RN 447406-03-3 HCAPLUS
CN 3-Quinolinecarboxamide, N-[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-3-[2-[methyl(phenylmethyl)amino]-2-oxoethyl]-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



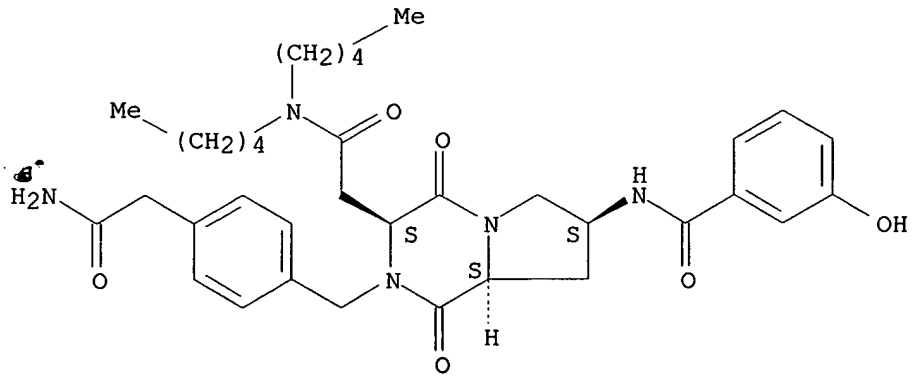
RN 447406-04-4 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-7-[(hydroxyacetyl)amino]-1,4-dioxo-N,N-dipentyl-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 447406-05-5 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-7-[(3-hydroxybenzoyl)amino]-1,4-dioxo-N,N-dipentyl-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

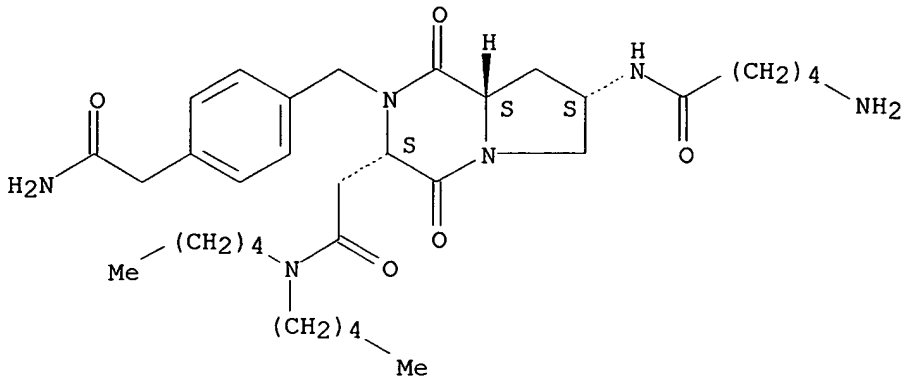
Absolute stereochemistry.



Searched by P. Ruppel

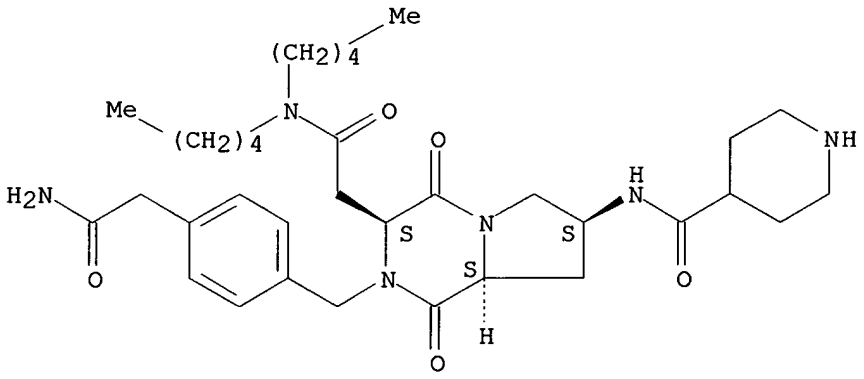
RN 447406-06-6 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-7-[(5-amino-1-oxopentyl)amino]octahydro-1,4-dioxo-N,N-dipentyl-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



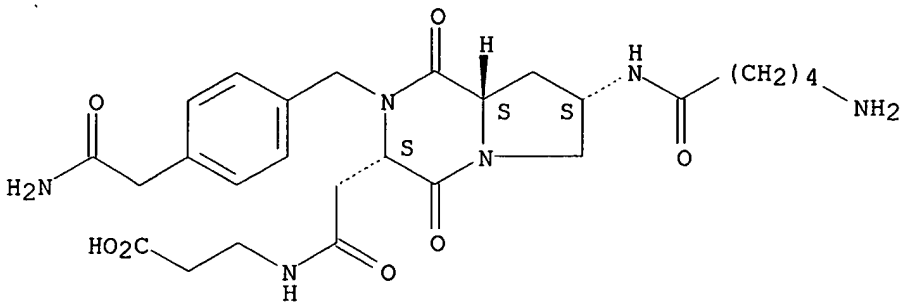
RN 447406-07-7 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-N,N-dipentyl-7-[(4-piperidinylcarbonyl)amino]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



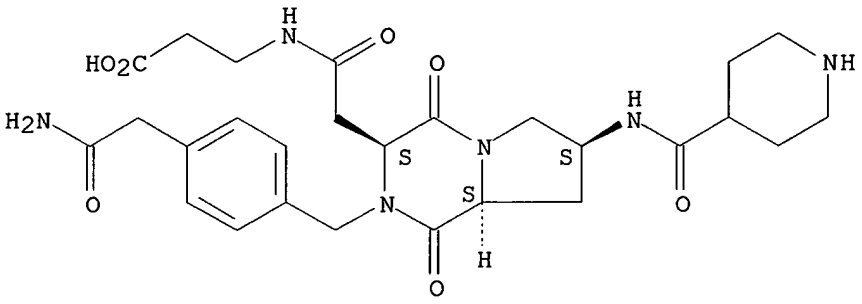
RN 447406-08-8 HCAPLUS
CN β-Alanine, N-[[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-7-[(5-amino-1-oxopentyl)amino]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-3-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



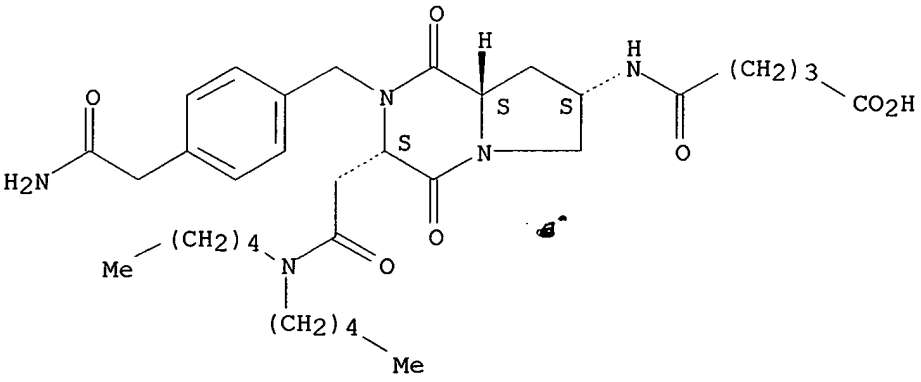
RN 447406-09-9 HCAPLUS
CN β-Alanine, N-[[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[(4-piperidinylcarbonyl)amino]pyrrolo[1,2-a]pyrazin-3-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 447406-10-2 HCAPLUS
CN Pentanoic acid, 5-[[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-3-[2-(dipentylamino)-2-oxoethyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]amino]-5-oxo- (9CI) (CA INDEX NAME)

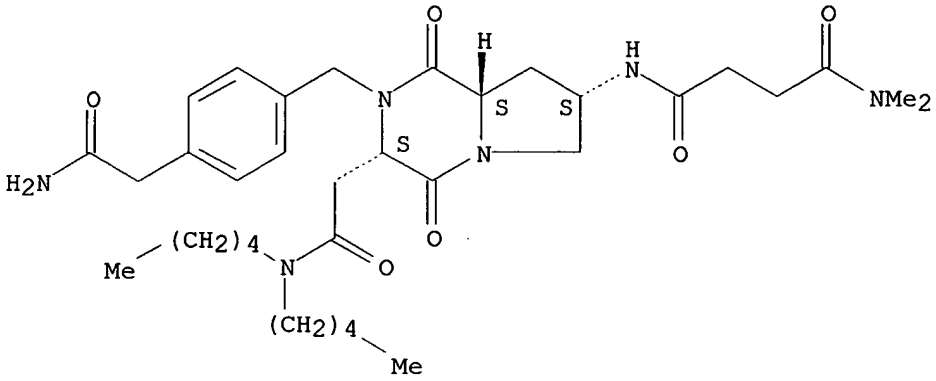
Absolute stereochemistry.



RN 447406-11-3 HCAPLUS

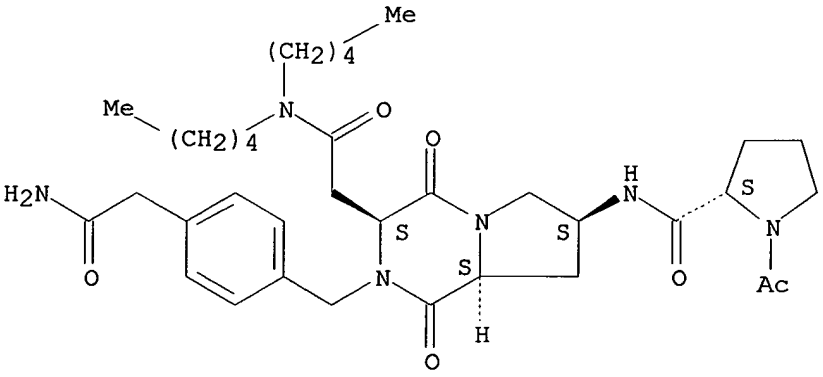
CN Butanediamide, N'-[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-3-[2-(dipentylamino)-2-oxoethyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



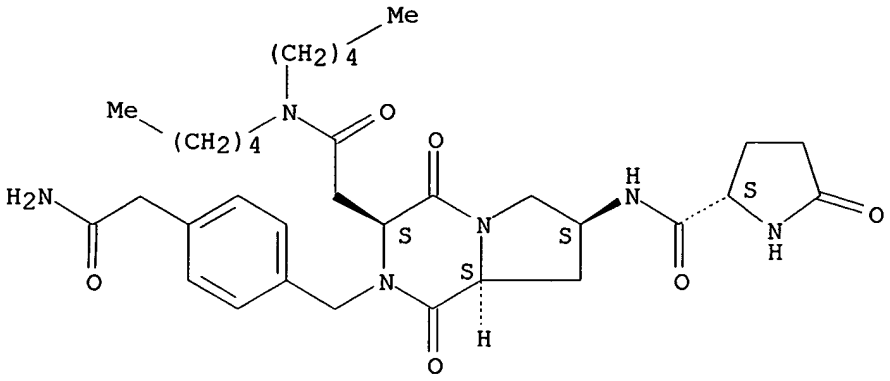
RN 447406-12-4 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 7-[[[(2S)-1-acetyl-2-pyrrolidinyl]carbonyl]amino]-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-N,N-dipentyl-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



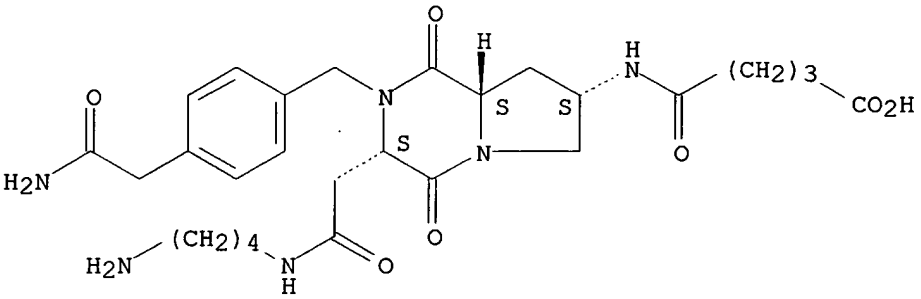
RN 447406-13-5 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[[[(2S)-5-oxo-2-pyrrolidinyl]carbonyl]amino]-N,N-dipentyl-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



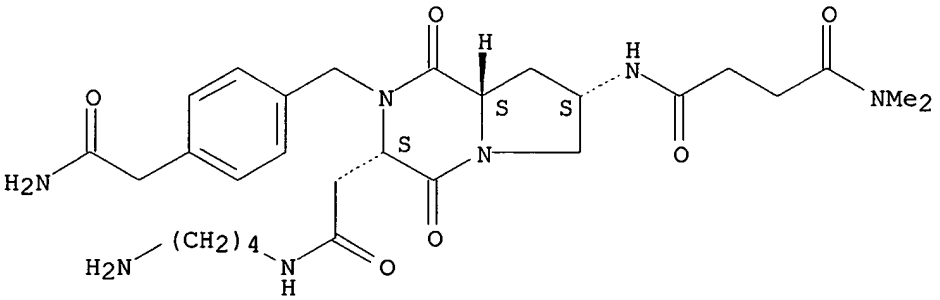
RN 447406-14-6 HCAPLUS
CN Pentanoic acid, 5-[[(3S,7S,8aS)-3-[2-[(4-aminobutyl)amino]-2-oxoethyl]-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]amino]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 447406-15-7 HCAPLUS
CN Butanediamide, N'-[(3S,7S,8aS)-3-[2-[(4-aminobutyl)amino]-2-oxoethyl]-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

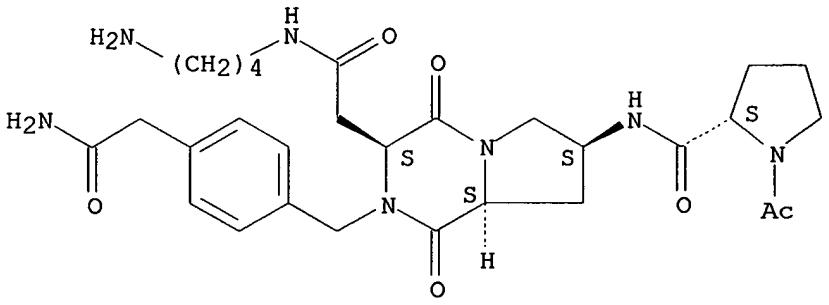
Absolute stereochemistry.



RN 447406-16-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 7-[[[(2S)-1-acetyl-2-

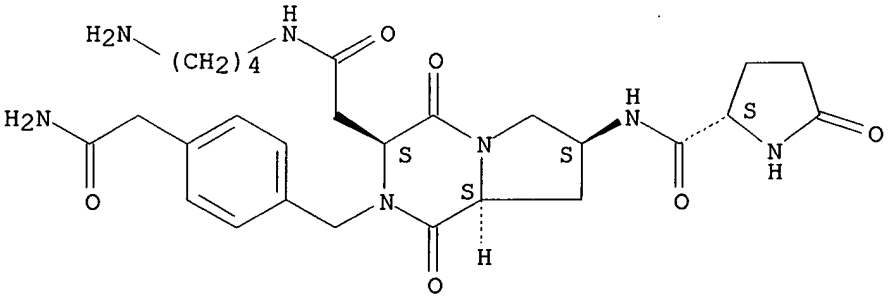
pyrrolidinyl]carbonyl]amino]-N-(4-aminobutyl)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



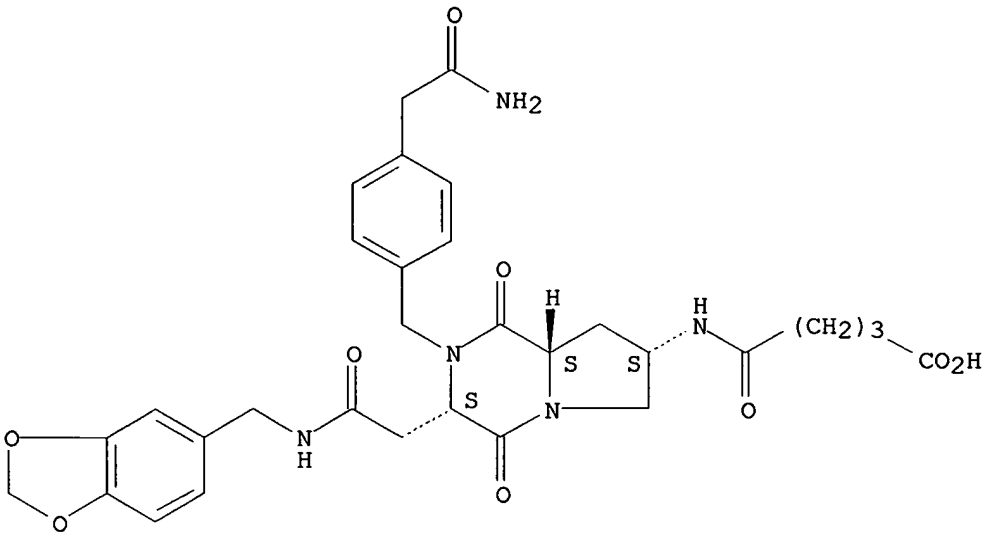
RN 447406-17-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, N-(4-aminobutyl)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[[[(2S)-5-oxo-2-pyrrolidinyl]carbonyl]amino]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



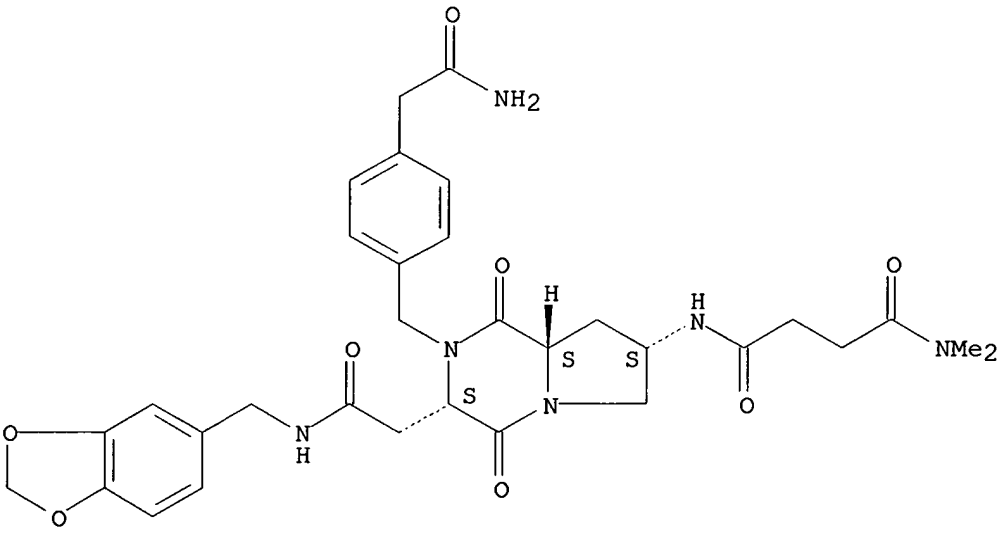
RN 447406-18-0 HCAPLUS
CN Pentanoic acid, 5-[[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-3-[2-[(1,3-benzodioxol-5-ylmethyl)amino]-2-oxoethyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]amino]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 447406-19-1 HCAPLUS
CN Butanediamide, N'-[(3S,7S,8aS)-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-3-[2-[(1,3-benzodioxol-5-ylmethyl)amino]-2-oxoethyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

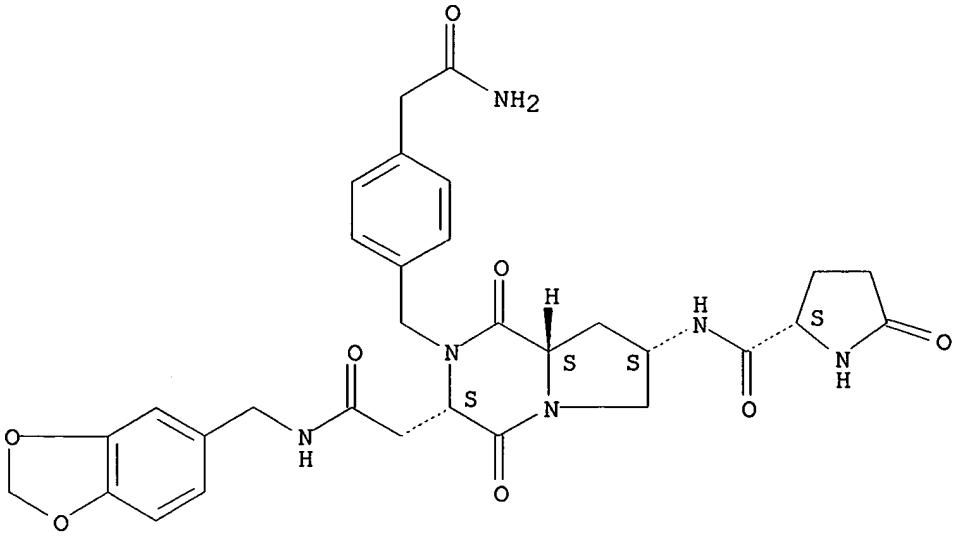
Absolute stereochemistry.



RN 447406-20-4 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, 2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]-N-(1,3-benzodioxol-5-ylmethyl)octahydro-1,4-dioxo-7-[[[(2S)-5-oxo-2-pyrrolidinyl]carbonyl]amino]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

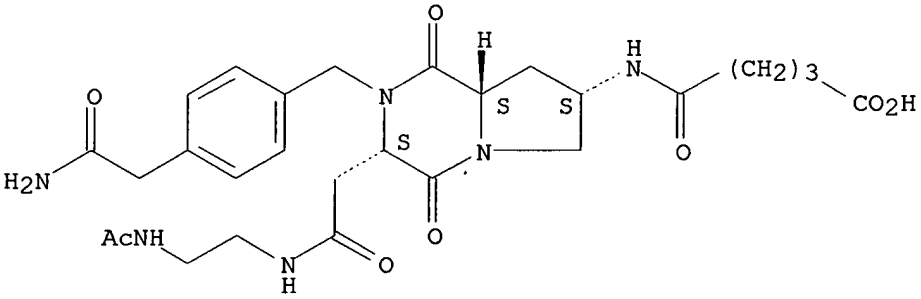
Absolute stereochemistry.

Searched by P. Ruppel



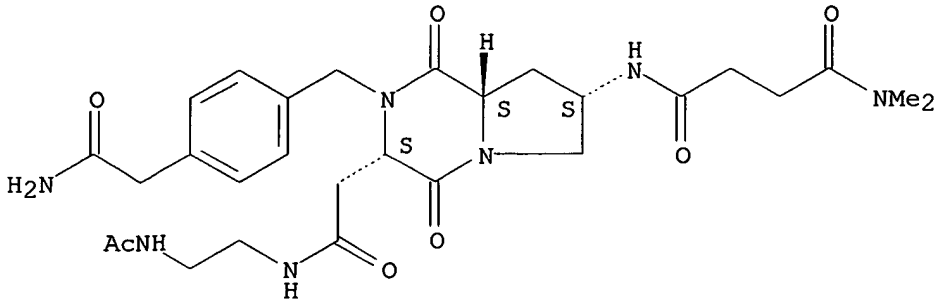
RN 447406-21-5 HCAPLUS
CN Pentanoic acid, 5-[[(3S,7S,8aS)-3-[2-[[2-(acetylamino)ethyl]amino]-2-oxoethyl]-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]amino]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



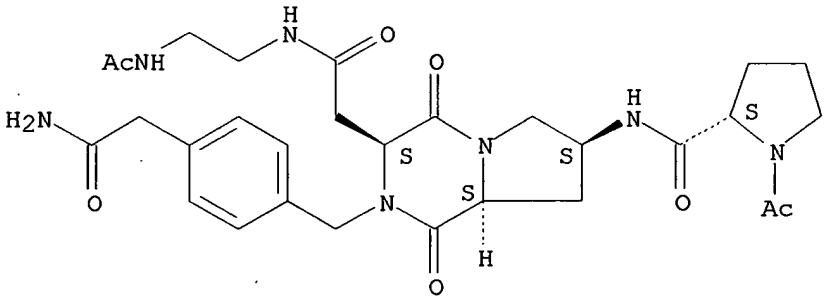
RN 447406-22-6 HCAPLUS
CN Butanediamide, N'-[(3S,7S,8aS)-3-[2-[[2-(acetylamino)ethyl]amino]-2-oxoethyl]-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxopyrrolo[1,2-a]pyrazin-7-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



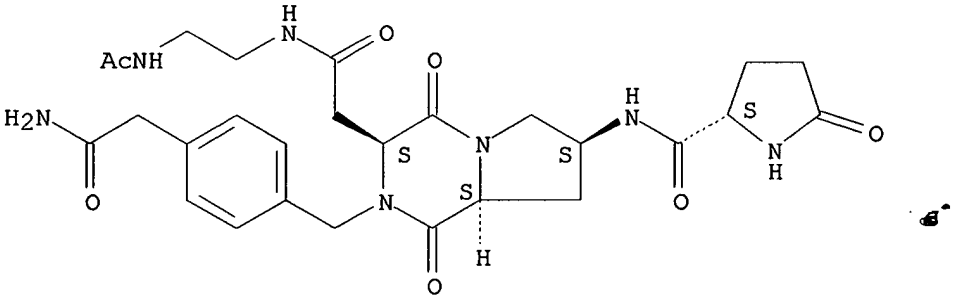
RN 447406-23-7 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, N-[2-(acetylamino)ethyl]-7-[[[(2S)-1-acetyl-2-pyrrolidinyl]carbonyl]amino]-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 447406-24-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetamide, N-[2-(acetylamino)ethyl]-2-[[4-(2-amino-2-oxoethyl)phenyl]methyl]octahydro-1,4-dioxo-7-[[[(2S)-5-oxo-2-pyrrolidinyl]carbonyl]amino]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **447405-83-6P 447405-85-8P 447405-87-0P 447405-88-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

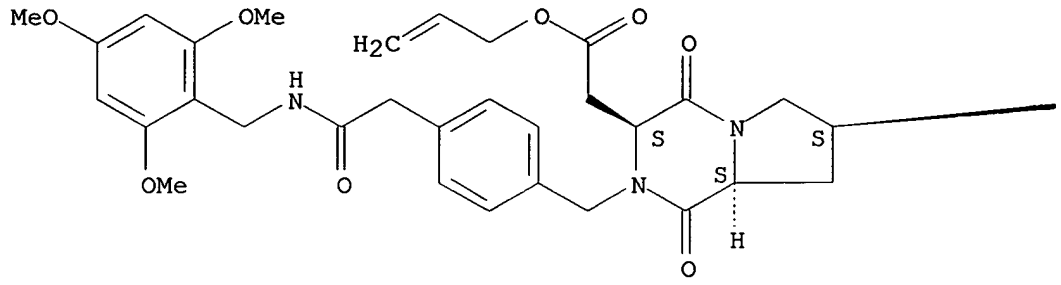
preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; preparation of pyrrolo[1,2-a]pyrazines as TNF-α inhibitors for treatment of inflammation)

RN 447405-83-6 HCAPLUS

CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 7-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]-, 2-propenyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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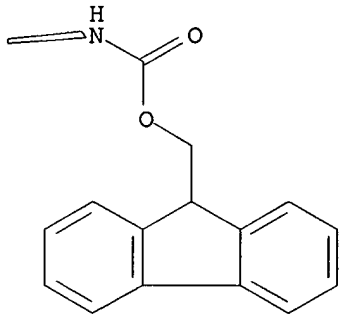

RN 447405-85-8 HCAPLUS

CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, octahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]-7-[(3-quinolinylcarbonyl)amino]-, 2-propenyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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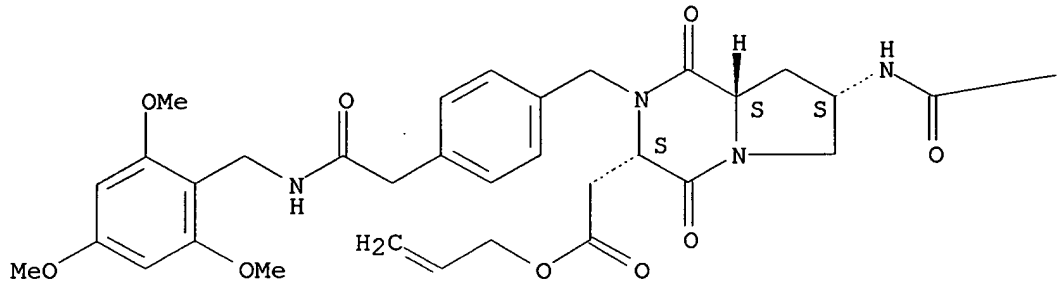

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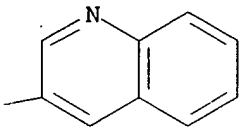
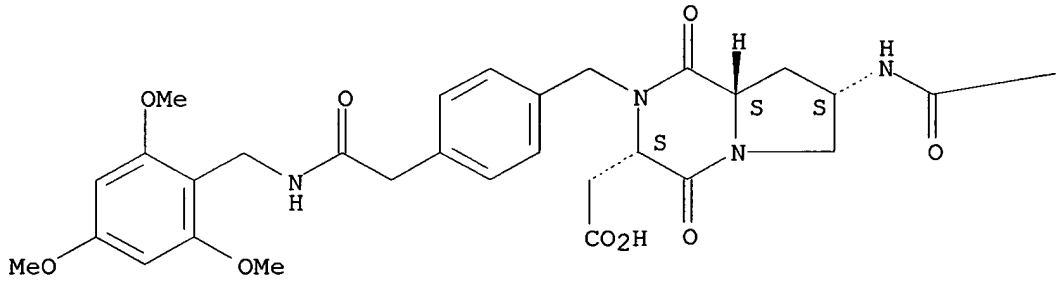


RN 447405-87-0 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, octahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]-7-[(3-quinolinylcarbonyl)amino]-, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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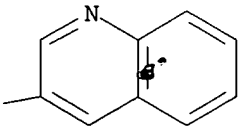
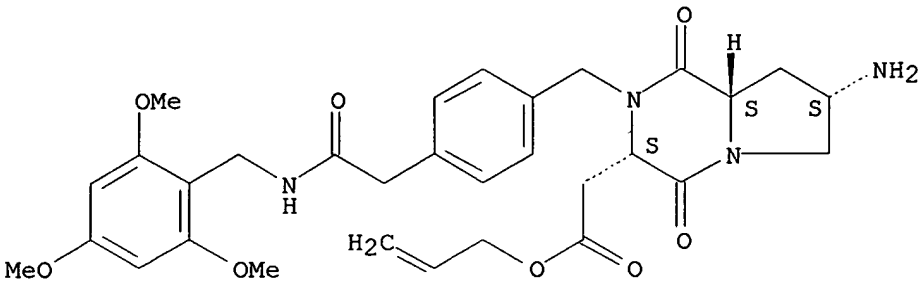


RN 447405-88-1 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 7-aminooctahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]-, 2-propenyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

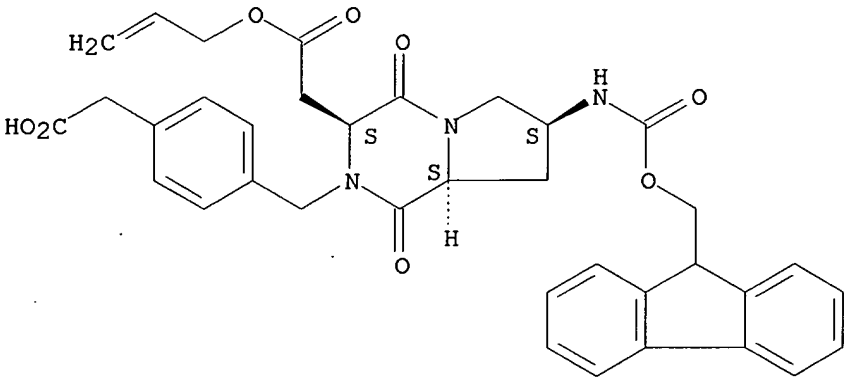
Absolute stereochemistry.



IT **447405-82-5P 447405-86-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrrolo[1,2-a]pyrazines as TNF-α inhibitors for treatment of inflammation)

RN 447405-82-5 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-acetic acid, 2-[[4-(carboxymethyl)phenyl]methyl]-7-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]octahydro-1,4-dioxo-, α-2-propenyl ester, (3S,7S,8aS)- (9CI) (CA INDEX NAME)

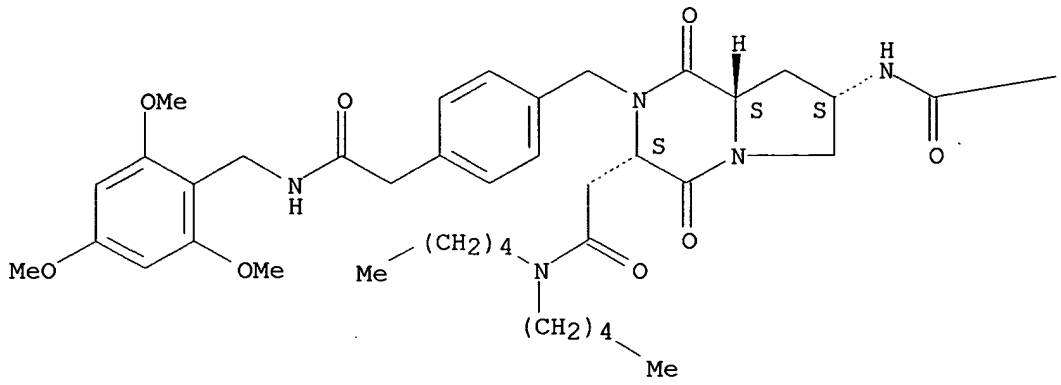
Absolute stereochemistry.



RN 447405-86-9 HCAPLUS
CN 3-Quinolinecarboxamide, N-[(3S,7S,8aS)-3-[2-(dipentylamino)-2-oxoethyl]octahydro-1,4-dioxo-2-[[4-[2-oxo-2-[[(2,4,6-trimethoxyphenyl)methyl]amino]ethyl]phenyl]methyl]pyrrolo[1,2-a]pyrazin-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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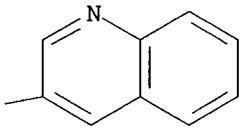


L6 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:46861 HCAPLUS
DOCUMENT NUMBER: 137:263280
TITLE: A new solid phase strategy for the preparation of hydroxyproline-based highly substituted diketopiperazines
AUTHOR(S): Bianco, Alberto; Furrer, Julien; Elbayed, Karim; Raya, Jesus; Briand, Jean-Paul
CORPORATE SOURCE: Laboratoire de Chimie Immunol., CNRS UPR 9021, Institut de Biologie Moleculaire et Cellulaire, Strasbourg, 67000, Fr.
SOURCE: Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemistry Diversity, Collected Papers, International Symposium, 6th, York, United Kingdom, Aug. 31-Sept. 4, 1999 (2001), Meeting Date 1999, 243-246. Editor(s): Epton, Roger. Mayflower Scientific Ltd.: Kingswinford, UK.
CODEN: 69CEGV; ISBN: 0-9515735-3-5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Two reaction pathways have been used for the synthesis of diketopiperazines (DKPs) from an N-protected hydroxyproline Me ester linked through the hydroxyl function to the Ellman resin. During the Cα -proline alkylation, two diastereoisomers are generally formed since this reaction is conducted at room temperature without any caution to control the diastereoselectivity. The conditions used for the alkylation of the amide bond generate four diastereoisomers due to racemization of the αCH-atom of the phenylalanine or leucine

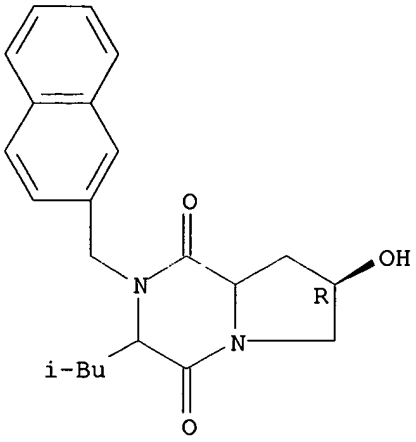
residue.

IT **269730-94-1P**
RL: BYP (Byproduct); PREP (Preparation)
(solid phase strategy for preparation of hydroxyproline-based highly substituted diketopiperazines)

RN 269730-94-1 HCAPLUS

CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-(2-methylpropyl)-2-(2-naphthalenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

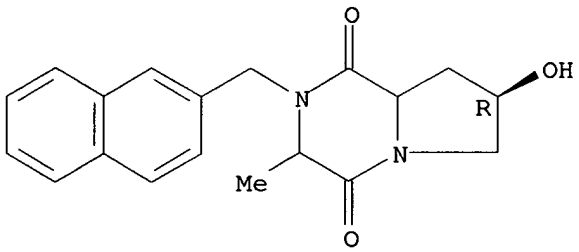


IT **269730-67-8P 269730-68-9P 269730-70-3P**
269730-75-8P 269730-89-4P 269730-90-7P
269730-92-9P 462656-54-8P 462656-55-9P
462656-56-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid phase strategy for preparation of hydroxyproline-based highly substituted diketopiperazines)

RN 269730-67-8 HCAPLUS

CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-methyl-2-(2-naphthalenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

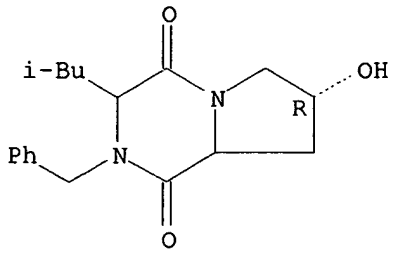
Absolute stereochemistry.



RN 269730-68-9 HCAPLUS

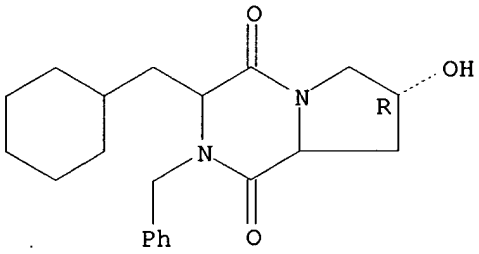
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-(2-methylpropyl)-2-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



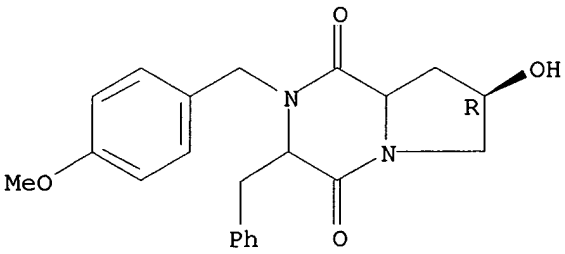
RN 269730-70-3 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 3-(cyclohexylmethyl)hexahydro-7-hydroxy-2-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



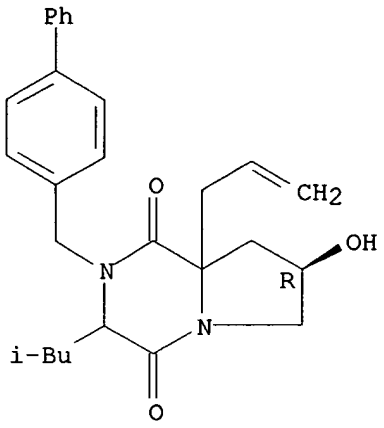
RN 269730-75-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-2-[(4-methoxyphenyl)methyl]-3-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



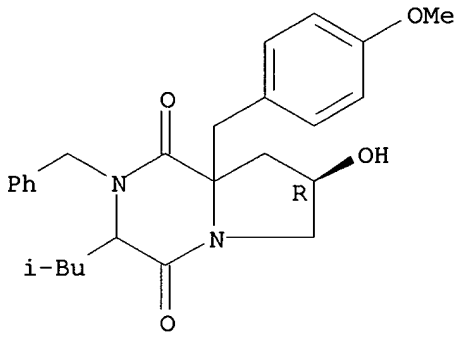
RN 269730-89-4 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 2-([1,1'-biphenyl]-4-ylmethyl)hexahydro-7-hydroxy-3-(2-methylpropyl)-8a-(2-propenyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



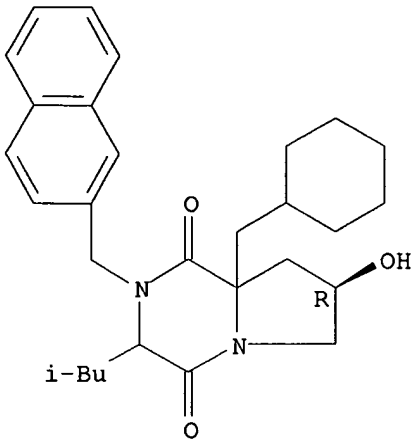
RN 269730-90-7 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-8a-[(4-methoxyphenyl)methyl]-3-(2-methylpropyl)-2-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



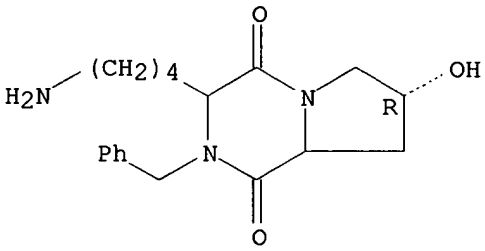
RN 269730-92-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 8a-(cyclohexylmethyl)hexahydro-7-hydroxy-3-(2-methylpropyl)-2-(2-naphthalenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



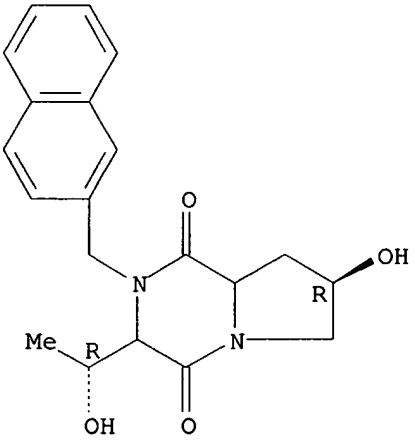
RN 462656-54-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 3-(4-aminobutyl)hexahydro-7-hydroxy-2-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



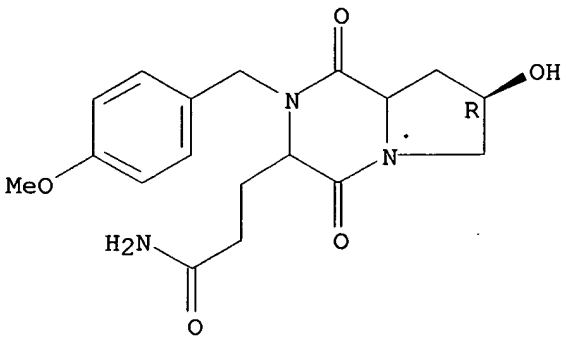
RN 462656-55-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-[(1R)-1-hydroxyethyl]-2-(2-naphthalenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



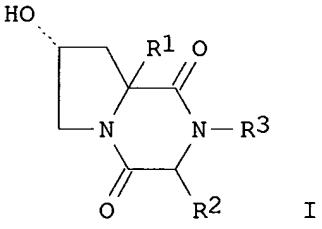
RN 462656-56-0 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-3-propanamide, octahydro-7-hydroxy-2-[(4-methoxyphenyl)methyl]-1,4-dioxo-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:167649 HCAPLUS
DOCUMENT NUMBER: 132:347890
TITLE: Solid-Phase Synthesis and Structural Characterization of Highly Substituted Hydroxyproline-Based 2,5-Diketopiperazines
AUTHOR(S): Bianco, Alberto; Sonksen, Carsten P.; Roepstorff, Peter; Briand, Jean-Paul
CORPORATE SOURCE: Laboratoire de Chimie Immunologique, Institut de Biologie Moleculaire et Cellulaire, Strasbourg, 67000, Fr.
SOURCE: Journal of Organic Chemistry (2000), 65(7), 2179-2187
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:347890
GI



I

AB Two general solid-phase methods for the synthesis of a new class of 2,5-diketopiperazines (DKPs), e.g., I (R1 = H, Me, PhCH2, allyl; R2 = H, Me, iso-Bu, PhCH2; R3 = 4-MeO-C6H4, PhCH2, allyl, Me), containing the

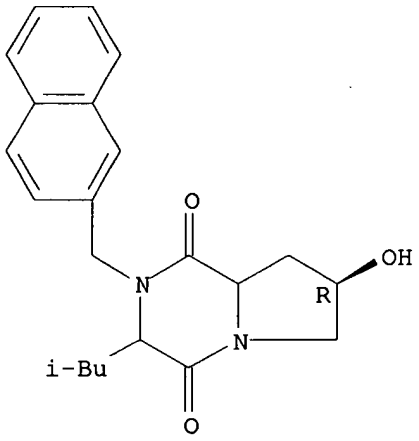
trans-4-hydroxy-L-proline amino acid residue (Hyp) have been developed. An N-protected hydroxyproline Me ester was linked through the hydroxyl function to the Ellman resin. The synthesis procedures were conceived to enable a sequence of Hyp alkylation, Hyp N-acylation, cyclization, and amide bond alkylation. Up to three different centers of mol. diversity were introduced around the DKP scaffold. Highly functionalized bicyclic compds. were obtained in good yield and purity. The alkylation of hydroxyproline αCH was performed without control of the diastereoselectivity. During the final alkylation of the backbone, amide bond epimerization at the α-carbon atoms of the two amino acid residues was observed The structures of representative DKPs were elucidated with multidimensional NMR expts. The described reaction pathways can be applied to the identification of heterocyclic mol. inhibitors to diverse enzyme targets.

IT **269730-94-1P**
RL: BYP (Byproduct); PREP (Preparation)
(solid-phase synthesis and structural characterization of highly substituted hydroxyproline-based diketopiperazines)

RN 269730-94-1 HCAPLUS

CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-(2-methylpropyl)-2-(2-naphthalenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

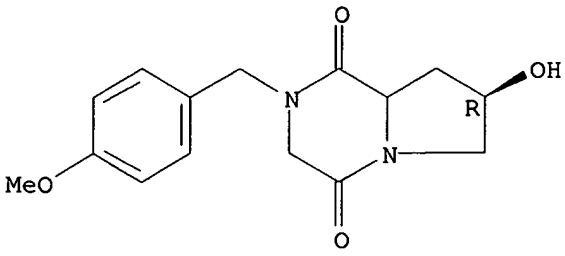


IT **269730-66-7P 269730-67-8P 269730-68-9P**
269730-70-3P 269730-75-8P 269730-89-4P
269730-90-7P 269730-92-9P 270082-50-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis and structural characterization of highly substituted hydroxyproline-based diketopiperazines)

RN 269730-66-7 HCAPLUS

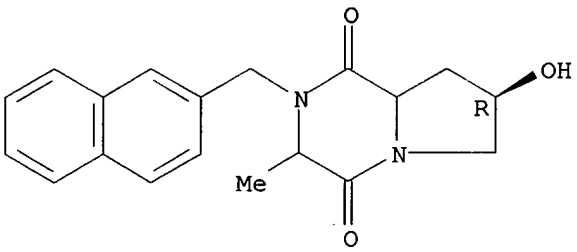
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-2-[(4-methoxyphenyl)methyl]-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



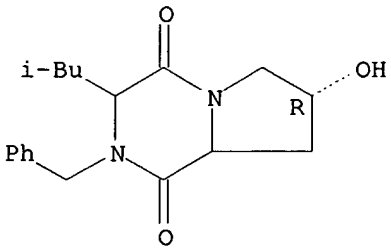
RN 269730-67-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-methyl-2-(2-naphthalenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



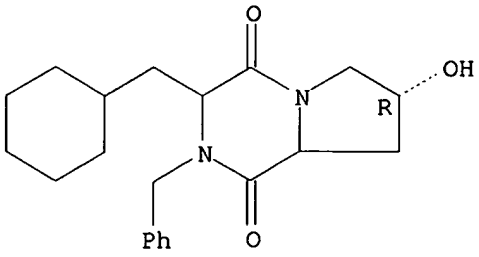
RN 269730-68-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-(2-methylpropyl)-2-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



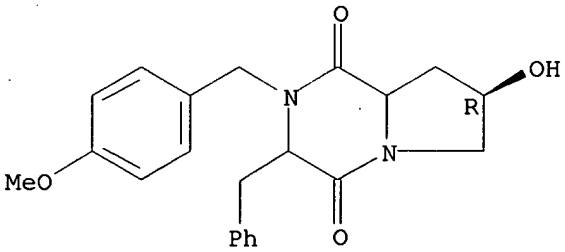
RN 269730-70-3 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 3-(cyclohexylmethyl)hexahydro-7-hydroxy-2-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



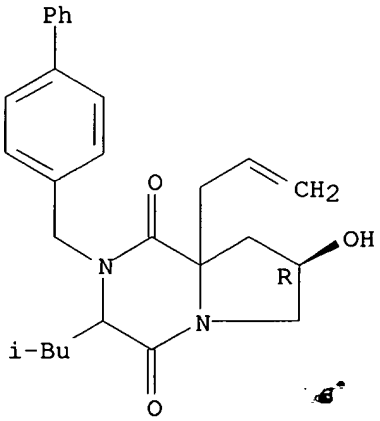
RN 269730-75-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-2-[(4-methoxyphenyl)methyl]-3-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



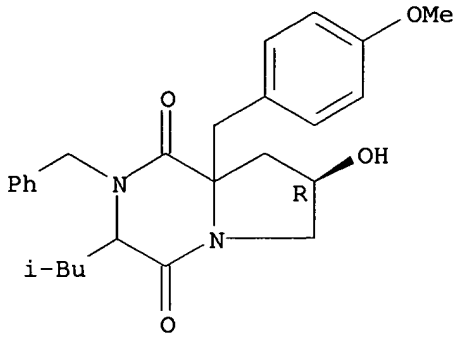
RN 269730-89-4 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 2-([1,1'-biphenyl]-4-ylmethyl)hexahydro-7-hydroxy-3-(2-methylpropyl)-8a-(2-propenyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



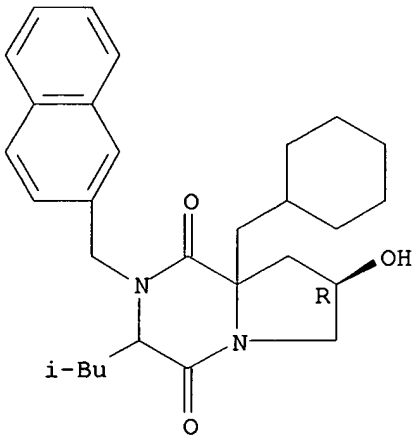
RN 269730-90-7 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-8a-[(4-methoxyphenyl)methyl]-3-(2-methylpropyl)-2-(phenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



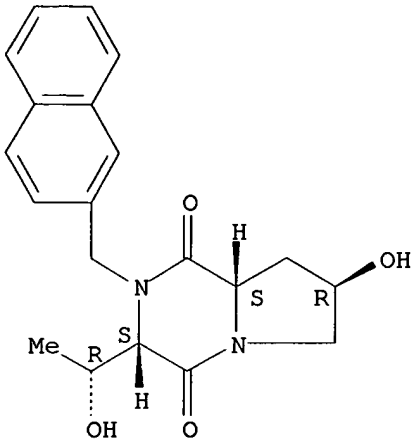
RN 269730-92-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 8a-(cyclohexylmethyl)hexahydro-7-hydroxy-3-(2-methylpropyl)-2-(2-naphthalenylmethyl)-, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 270082-50-3 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-3-[(1R)-1-hydroxyethyl]-2-(2-naphthalenylmethyl)-, (3S,7R,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

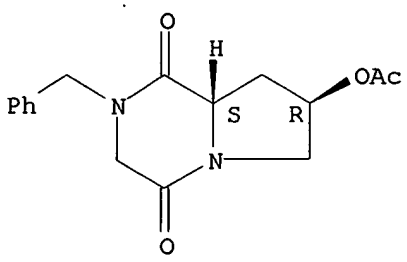
L6 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:143351 HCAPLUS
DOCUMENT NUMBER: 114:143351
TITLE: 8-Hydroxylated derivatives of diazabicyclo[4.3.0]nonanes, 2,5-dioxodiazabicyclo[4.3.0]nonanes and some related esters
AUTHOR(S): Diafi, Lahcen; Couquelet, Jacques; Tronche, Pierre; Gardette, Daniel; Gramain, Jean Claude
CORPORATE SOURCE: Groupe Rech. Pharmacochim., Fac. Pharmacie, Clermont-Ferrand, 63001, Fr.
SOURCE: Journal of Heterocyclic Chemistry (1990), 27(7), 2181-7
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:143351

AB The title compds. were prepared from trans-4-hydroxyl-L-proline. Esterification with appropriate anhydrides led to the corresponding esters with 6S,8R configuration. Inversion of configuration at C-8 was performed using Mitsunobu method and led to the diastereoisomer series of 6S,8S esters.

IT **132714-99-9P 132715-00-5P 132715-02-7P**
132715-03-8P 132715-05-0P 132715-06-1P
132749-00-9P 132749-02-1P 132749-04-3P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and spectra of)

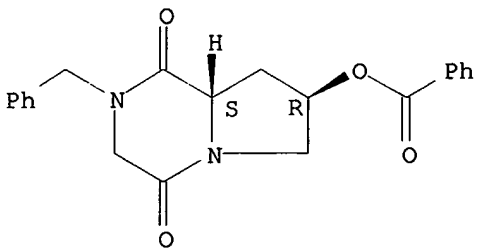
RN 132714-99-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 7-(acetyloxy)hexahydro-2-(phenylmethyl)-, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



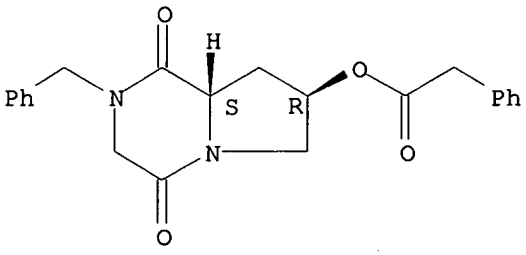
RN 132715-00-5 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 7-(benzoyloxy)hexahydro-2-(phenylmethyl)-, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



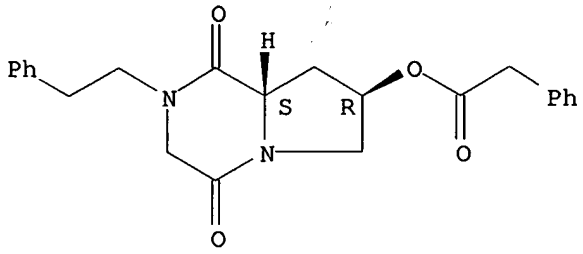
RN 132715-02-7 HCAPLUS
CN Benzeneacetic acid, octahydro-1,4-dioxo-2-(phenylmethyl)pyrrolo[1,2-a]pyrazin-7-yl ester, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



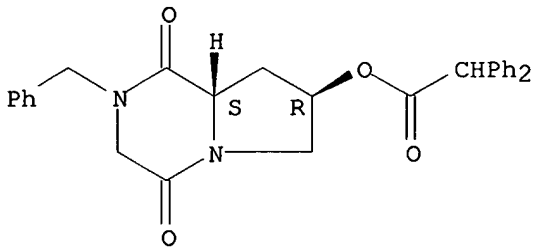
RN 132715-03-8 HCAPLUS
CN Benzeneacetic acid, octahydro-1,4-dioxo-2-(2-phenylethyl)pyrrolo[1,2-a]pyrazin-7-yl ester, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



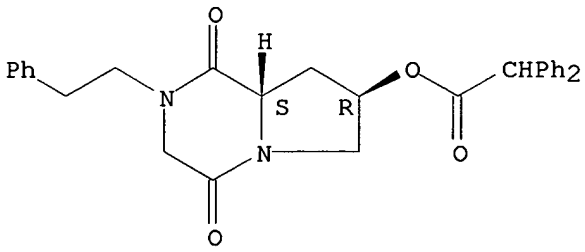
RN 132715-05-0 HCAPLUS
CN Benzeneacetic acid, α-phenyl-, octahydro-1,4-dioxo-2-(phenylmethyl)pyrrolo[1,2-a]pyrazin-7-yl ester, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



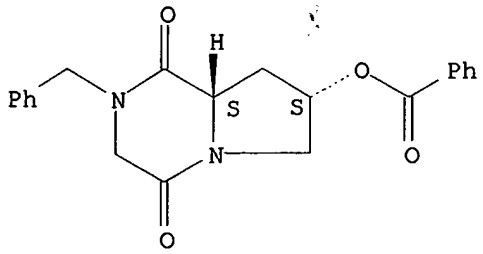
RN 132715-06-1 HCAPLUS
CN Benzeneacetic acid, α-phenyl-, octahydro-1,4-dioxo-2-(2-phenylethyl)pyrrolo[1,2-a]pyrazin-7-yl ester, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



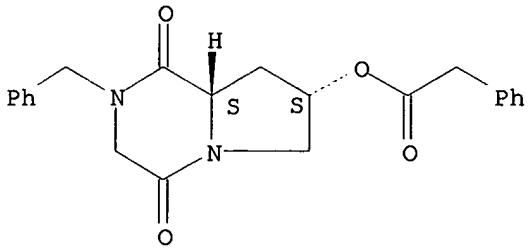
RN 132749-00-9 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, 7-(benzoyloxy)hexahydro-2-(phenylmethyl)-, (7S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



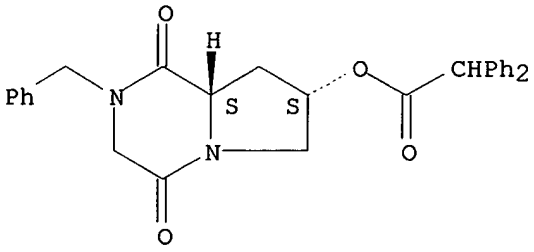
RN 132749-02-1 HCAPLUS
CN Benzeneacetic acid, octahydro-1,4-dioxo-2-(phenylmethyl)pyrrolo[1,2-a]pyrazin-7-yl ester, (7S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



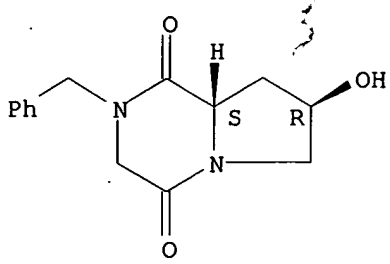
RN 132749-04-3 HCAPLUS
CN Benzeneacetic acid, α-phenyl-, octahydro-1,4-dioxo-2-(phenylmethyl)pyrrolo[1,2-a]pyrazin-7-yl ester, (7S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



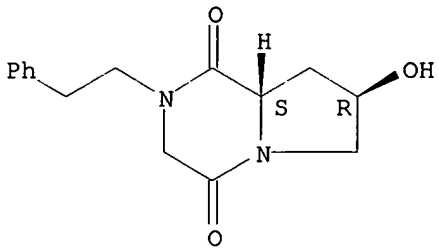
IT **132714-97-7P 132714-98-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, spectra and reactions of)
RN 132714-97-7 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-2-(phenylmethyl)-, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 132714-98-8 HCAPLUS
CN Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-7-hydroxy-2-(2-phenylethyl)-, (7R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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